## REMARKS

Claims 28, 29, 33 - 38 and 40 - 52 are pending. Claims 28, 29, 48 and 49 have been amended. Claims 1 - 27, 30 – 34, 36, 39 and 52 were cancelled. New claims 53 – 58 have been added. No new matter has been added by virtue of the new claims and amendments, support being found throughout the specification and claims as originally filed.

Specifically, support for the new claims and amendments to the claims, in particular support for the microfluidic system as presently claimed used in conjunction with the sensors as claimed can be found in the specification, for example at page 17 – 19. Figure 5 shows the overall chip structure for the microfluidic system. 5B shows an enlarged view of the reservoirs of the chip and their individual connecting channels and Figure 5C shows an enlarged view of interdigitating microchannel whose outlets intersect with the sensor chamber of the chip. (Fig 5 and page 7). Fig 6 B – G shows enlarged views of the outlets of microchannels and their positions with respect to a superfusion capillary and a sensor. (Fig 6 and page 7 – 8). Fig 7 shows a microfluidic chip for carrying out exchange of fluids around a patch clamped cell. Fig 7A shows channels feeding into a cell chamber. (Fig 7 and page 8).

Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

### Objections

### Drawings

The Examiner has objected to the Drawings filed on October 8, 2003.

Applicants submit replacement drawings with this response and respectfully request that the objection be withdrawn.

**Claim Rejections Withdrawn**

**35 U.S.C. §112, second paragraph**

The Examiner has withdrawn the rejection to claim 51 under 35 U.S.C. §112, second paragraph, as being indefinite.

**Claim Rejections**

**35 U.S.C. §102(e)**

Claims 28, 29, 33, 36 – 38, 40, 48, 49, 51 and 52 were rejected under 35 U.S.C. 102(e) as being anticipated by Benavides et al. (US 6,443,179; the '179 reference herein). Applicants respectfully traverse the rejection.

As amended, the claims recite systems where a macroscale device is interfaced with a microfluidic device, where a stable association is formed between the microfluidic device and the macroscale device, wherein the microfluidic device has a plurality of microchannels suitable for containing a fluid stream; and at least one sensor chamber containing at least one sensor, wherein each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chamber, and wherein the microchannels correspond in number to the number of wells in a microtiter plate.

In order to anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure, § 2131.

The '179 reference does not anticipate the invention as claimed. In particular, the '179 reference nowhere teaches or suggests a microfluidic device, let alone a system, comprising a macroscale device which is interfaced with a microfluidic device as claimed, where **the microfluidic device has a plurality of microchannels suitable for containing a fluid stream**; and **at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chamber**.

The Examiner argues that the '179 reference teaches "a macroscale device…which is interfaced with a microfluidic device using double sided tape or transfer tape to form a

stable association between the microfluidic device and the macroscale device…wherein the microfluidic device has at least one microchannel suitable for containing a fluid stream." The Examiner points to Figure 21 as an example of such a device. Nowhere in the '179 reference, or in Figure 21 is the present invention taught or suggested.

The '179 reference is directed to architecture for packaging surface micromachined electro-microfluidic devices. The '179 reference teaches an electromicrofluidic package that can be plugged into a fluidic printed wiring board, and that uses electric and fluidic connections (col 4, lines 36 – 50). According to the '179 reference "(t)he larger package consists of a circuit board with embedded fluidic channels and standard fluidic connectors…(and) (t)he embedded channels connect to the smaller package, an Electro-Microfluidic Dual-Inline-Package (EMDIP) that takes fluid to the microfluidic integrated circuit (MIC)." (see, e.g. abstract). The '179 reference teaches fluidic and electrical connections to surface micromachined electro-microfluidic devices, where fluidic connections are made through holes in the EMDIP that coincide with holes extending through the Microfluidic Integrated circuit (MIC) from back to front that connect to surface micromachined channels on the front of the module. (col 7, line 6).

Figure 21, as pointed out by the Examiner, and shown below, teaches a device that is clearly different from the present invention. Nowhere does Figure 21, or any of the other Figures, show a microfluidic device with a plurality of microchannels suitable for containing a fluid stream, at least one sensor chamber containing at least one sensor, and where each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chamber.

Figure 21

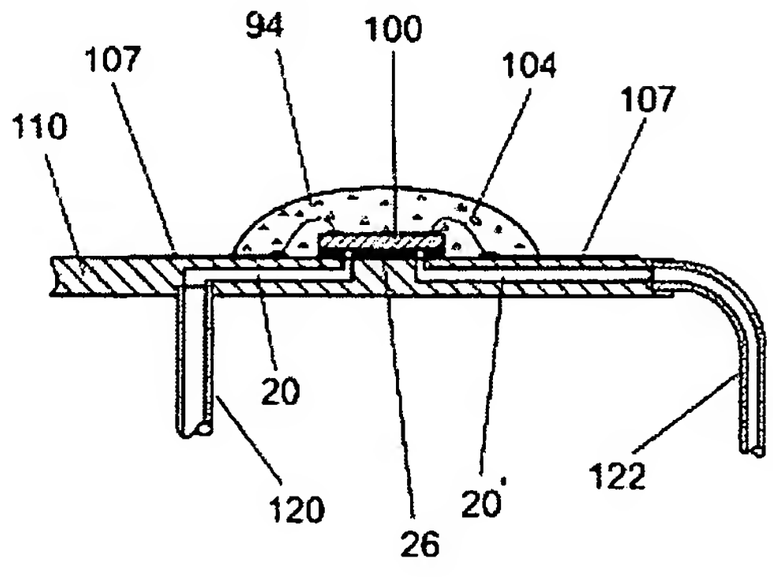


Figure 21 shows an "assembly 15 (that) comprises an electro-microfluidic device 100 attached directly to a fluidic printed wiring board (FPWB) 110. An adhesive gasket 26 provides combined mechanical bonding and fluidic coupling between fluidic inlet and outlet ports on the bottom side of device 100 (e.g. ports 101), and fluidic channels 20 and 20' disposed inside of FPWB 110. Assembly 15 can further comprise microcapillary glass tube 120 attached to the backside of FPWB 110 and fluidically coupled to channel 20." (col. 17, line 12).

Nowhere in the description or in any of the figures of the '179 reference is there teaching or suggestion that the microfluidic device, which the Examiner argues is the chip (100), has a **plurality of microchannels suitable for containing a fluid stream**; and wherein the microfluidic device has at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a **substantially separate aqueous stream into the sensor chamber**, as taught in the present invention.

Accordingly, Applicants request withdrawal of the rejection and allowance of the claims.

**35 U.S.C. §103 (a)**

Claims 34 and 35 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Benavides (the '179 reference, as above) in view of Pfost et al. (the '621 reference). Applicants respectfully traverse the rejection.

As set forth above, the claims recite systems where a macroscale device is interfaced with a microfluidic device, where a stable association is formed between the microfluidic device and the macroscale device, wherein the microfluidic device has a plurality of microchannels suitable for containing a fluid stream; and at least one sensor chamber containing at least one sensor, and wherein each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chamber.

Claims 34 and 35 have been cancelled to facilitate prosecution and allowance of this application.

Accordingly, Applicants respectfully request that the foregoing rejection be withdrawn.

Claims 41 - 43 and 35 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Benavides (the '179 reference, as above) in view of Bjornson et al. (6,103,199; the '199 reference). Applicants respectfully traverse this rejection.

Claims 44, 45, 49 and 50 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Benavides (the '179 reference, as above) in view of Crandall et al. (6,352,766; the '766 reference). Applicants respectfully traverse this rejection.

Claims 46 and 47 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Benavides (the '179 reference, as above) in view of DiZio et al. (6,455,152; the '152 reference). Applicants respectfully traverse this rejection.

Because all of the foregoing rejections rely on the primary reference Benavides (the '179 reference), in combination with secondary references, these rejections will be addressed together.

As set forth above, nowhere in the '179 reference is there teaching or suggestion of a microfluidic device with **a plurality of microchannels suitable for containing a fluid stream**; wherein the microfluidic device has at least one sensor chamber containing at least one sensor, and **wherein each microchannel comprises an outlet for delivering a**

**substantially separate aqueous stream into the sensor chamber**, as taught in the present invention.

None of the '199, '766 or '152 references cures the defects of the '179 reference.

The '179 reference provides no teaching or motivation to provide a microfluidic substrate that comprises a plurality of microchannels where each microchannel comprises an outlet for delivering a substantially separate aqueous stream into a sensor chamber. As set forth above, the '179 reference features architecture for packaging surface micromachined electro-microfluidic devices. The '179 reference is directed to a need for a standardized electromicrofluidic package that can be plugged into a standard electrical printed circuit board. (col. 4, line 36 – 40). The '179 reference nowhere teaches or suggests microfluidic devices as presently claimed.

None of the '199, '766 or '152 references, when combined with the '179 reference, teaches the invention as claimed. None of the '199, '766 or '152 references teach or suggest a microfluidic device with **a plurality of microchannels suitable for containing a fluid stream**; wherein the microfluidic device has at least one sensor chamber containing at least one sensor, and **wherein each microchannel comprises an outlet for delivering a substantially separate aqueous stream into the sensor chamber**, as taught in the present invention.

Accordingly, Applicants request withdrawal of the rejection and allowance of the claims.

**Double Patenting**

The Examiner argues that if claims 28 and 29 are found allowable, then claims 48 and 49 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. The Examiner argues that "when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim." (Office Action, p.9). Applicants respectfully traverse the rejection.

The claims are directed to different embodiments, and are not unnecessarily duplicative.

In the interest of advancing prosecution, should claims 28 and 29 be allowed, applicants would consider amending or cancelling any claims that would be duplicates of the allowed claims under 37 CFR 1.75.

## CONCLUSION

In light of the above remarks, Applicants respectfully request early consideration and allowance of the subject application.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment to Deposit Account No. 04-1105.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: March 5, 2009

Respectfully submitted,

By _____

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